

REMARKS

The fee for a one-month extension of time and any other fees that may be due in connection with the filing of this paper or with this application should be charged to Deposit Account No. 02-1818. If a Petition for extension of time is needed, this paper is to be considered such Petition.

Claims 1-25, 27-35, 62-70, 72-78 and 82-86 are pending. Claims 69, 70 and 72-77 are withdrawn but are retained for possible joinder if claim 1 is deemed allowable.

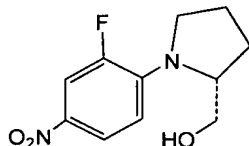
Claims 1, 2, 6, 7, 28-30 and 62 are amended and claims 83-86 are added. Claim 1 is amended to delete hydrogen an optionally substituted C₁-C₄ alkyl as a selection in the definition of substituent R². Claim 1 also is amended to correct an inadvertent typographical in which the selections COR^A and CO₂R^A were omitted from the definition of R⁹. Basis for the amendment can be found, *e.g.*, in original claim 2 as filed and at page 4, line 18. Claims 2, 6, 7, 28, 29 and 62 are amended to comport with amended claim 1. Claim 30 is amended to be an independent claim including limitations of its previous base claims and to correct a grammatical error.

Basis for new claim 83 is found in the original claims as filed and in the specification at, *e.g.*, pages 27-45. Basis for new claim 84 is found, *e.g.*, in original claim 62 and in the specification at pages 56-58. Basis for new claims 85 and 86 is found in original claim 78. No new matter is added.

I. THE REJECTION OF CLAIMS UNDER 35 U.S.C. §102(b)

1. Selvakumar *et al.*

Claims 1-4 and 12-16 are rejected under 35 U.S.C. 102(b) as being anticipated by RN 509151-85-3 CAPLUS (Selvakumar *et al.* (Synthesis 16: 2421-2425 (2002))), because Selvakumar *et al.* discloses the following compound:



Reconsideration of the grounds for the rejection respectfully is requested in view of the amendments herein and the following remarks.

RELEVANT LAW

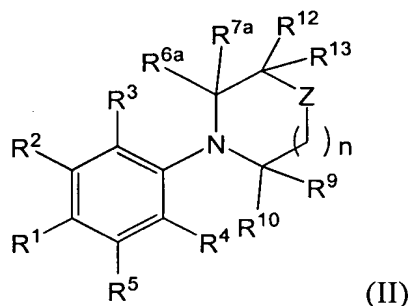
Anticipation requires the disclosure in a single prior art reference of each element of the claim under consideration. *In re Spada*, 15 USPQ2d 1655 (Fed. Cir., 1990), *In re Bond*, 15 USPQ 1566 (Fed. Cir. 1990), *Soundscriber Corp. v. U.S.*, 360 F.2d 954, 148 USPQ 298, 301, adopted 149 USPQ 640 (Ct. Cl.) 1966. See, also, *Richardson v. Suzuki Motor Co.*, 868

F.2d 1226, 1236, 9 USPQ2d 1913,1920 (Fed. Cir.), *cert. denied*, 110 S.Ct. 154 (1989).

"[A]ll limitations in the claims must be found in the reference, since the claims measure the invention." *In re Lang*, 644 F.2d 856, 862, 209 USPQ 288, 293 (CCPA 1981). It is incumbent on Examiner to identify wherein each and every facet of the claimed invention is disclosed in the reference. *Lindemann Maschinen-fabrik GmbH v. American Hoist and Derrick Co.*, 730 F.2d 1452, 221 USPQ 481 (Fed. Cir. 1984). Further, the reference must describe the invention as claimed sufficiently to have placed a person of ordinary skill in the art in possession of the invention. *In re Oelrich*, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981).

THE CLAIMS

Claim 1 recites a compound of formula II:



where:

R¹ is selected from among SR^A, NO₂, CN, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, COR^A, CO₂R^A, CONR^AR^B, SOR^A, and SO₂R^A;

R² is selected from among F, Cl, Br, I, OR^A, SR^A, NO₂, CN, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, COR^A, CO₂R^A, CONR^AR^B, SOR^A, SO₂R^A, and SO₂NR^AR^B, NHCOR^A, and NHCONR^AR^B;

R³, R⁴, and R⁵ each independently is selected from among hydrogen, F, Cl, OR^A, an optionally substituted C₁-C₄ alkyl, and an optionally substituted C₁-C₄ haloalkyl; provided that if R¹ is NO₂ and R³ is F, then Z is not O;

R^{6a} and R^{7a} each independently is selected from among hydrogen, an optionally substituted C₁-C₆ alkyl, an optionally substituted C₁-C₆ haloalkyl, an optionally substituted C₁-C₆ heteroalkyl, an optionally substituted C₂-C₆ alkynyl, and an optionally substituted C₂-C₆ alkenyl; or R^{6a} and R^{7a} together form a carbonyl;

R⁹ is selected from an optionally substituted C₁-C₈ alkyl, an optionally substituted C₂-C₈ alkenyl, an optionally substituted C₁-C₈ haloalkyl, an optionally substituted C₂-C₈ haloalkenyl, C₁-C₈ heteroalkyl, an optionally substituted C₂-C₈ heteroalkenyl, an optionally substituted C₂-C₈ alkynyl, an optionally substituted C₂-C₈ haloalkynyl, an optionally substituted C₂-C₈ heteroalkynyl, an optionally substituted aryl, an optionally substituted heteroaryl, CH(R^D)OR^A, CH(R^D)NR^AR^B, COR^A, CO₂R^A, and (CH₂)_mR^C;

R¹⁰ is selected from among hydrogen, an optionally substituted C₁-C₆ alkyl, an optionally substituted C₁-C₆ haloalkyl, an optionally substituted C₁-C₆ heteroalkyl, an optionally substituted C₂-C₆ alkynyl, and an optionally substituted C₂-C₆ alkenyl;

R¹² and R¹³ each independently is selected from among hydrogen, F, Cl, OR^A, NR^AR^B, SR^A, an optionally substituted C₁-C₆ alkyl, an optionally substituted C₁-C₆ haloalkyl, an optionally substituted C₁-C₆ heteroalkyl, an optionally substituted C₂-C₆ alkynyl, an optionally substituted C₂-C₆ alkenyl, and (CH₂)_mR^C;

R^A and R^B each independently is selected from among hydrogen, an optionally substituted C₁-C₄ alkyl, an optionally substituted C₁-C₄ haloalkyl, and an optionally substituted C₁-C₄ heteroalkyl;

R^C is selected from among an optionally substituted aryl and an optionally substituted heteroaryl that is optionally substituted with a substituent selected from among F, Cl, Br, I, CN, OR^A , NO_2 , $NR^A R^B$, SR^A , SOR^A , $SO_2 R^A$, an optionally substituted C_1 - C_4 alkyl, an optionally substituted C_1 - C_4 haloalkyl, and an optionally substituted C_1 - C_4 heteroalkyl;

R^D is selected from among hydrogen, an optionally substituted C_1 - C_4 alkyl, an optionally substituted C_1 - C_4 haloalkyl, and an optionally substituted C_1 - C_4 heteroalkyl;

Z is selected from among O, S, $CR^A R^B$, and NR^D ;

n is 0, 1, or 2; and

m is 1 or 2;

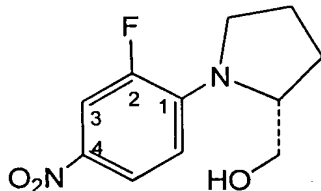
or a pharmaceutically acceptable salt, ester, or amide thereof.

Claims 2-4 and 12-16 depend from claim 1 and include every limitation thereof.

DISCLOSURE OF THE CITED ART

Selvakumar *et al.* describes Smiles rearrangements in certain alkyl aryl nitro compounds having a NH_2 group as the nucleophile and oxygen as the leaving group.

Selvakumar *et al.* describes an intermediate having the structure:



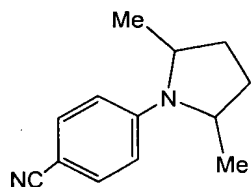
in the formation of aromatic tricyclic compounds. Selvakumar *et al.* does not disclose any compound that includes a 1-phenylpyrrolidine core structure substituted at position 3 of the aromatic ring with a non-hydrogen substituent.

ANALYSIS

The cited compound of Selvakumar *et al.* is not within the scope of any of claims 1-4 or 12-16 or any pending claim. The compounds of instant formula II include a non-hydrogen substituent selected from among F, Cl, Br, I, OR^A , SR^A , NO_2 , CN, an optionally substituted C_1 - C_4 haloalkyl, an optionally substituted C_1 - C_4 heteroalkyl, COR^A , $CO_2 R^A$, $CONR^A R^B$, SOR^A , $SO_2 R^A$, and $SO_2 NR^A R^B$, $NHCOR^A$, and $NHCONR^A R^B$ at position 3 of the aromatic ring. The cited compound of Selvakumar *et al.* has a hydrogen substituent at the corresponding position. None of the compounds of Selvakumar *et al.* has a non-hydrogen substituent selected from among F, Cl, Br, I, OR^A , SR^A , NO_2 , CN, an optionally substituted C_1 - C_4 haloalkyl, an optionally substituted C_1 - C_4 heteroalkyl, COR^A , $CO_2 R^A$, $CONR^A R^B$, SOR^A , $SO_2 R^A$, and $SO_2 NR^A R^B$, $NHCOR^A$, and $NHCONR^A R^B$ at position 3 of the aromatic ring. Thus, neither the cited compound of RN 509151-85-3 CAPLUS nor any compound described in Selvakumar *et al.* includes every element of claims 1-4 and 12-16. Therefore, Selvakumar *et al.* does not anticipate any of claims 1-4 and 12-16 or any pending claim.

2. Rettig *et al.*

Claims 5 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by RN 80887-45-2 CAPLUS (Rettig *et al.* (Journal of Physical Chemistry 89(22): 4676-4680 (1985)), because Rettig *et al.* discloses the following compound:



Reconsideration of the grounds for the rejection respectfully is requested in view of the amendments herein and the following remarks.

RELEVANT LAW

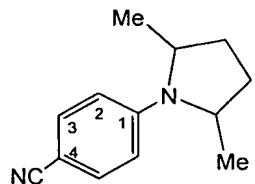
See related section above.

THE CLAIMS

Claims 5 and 17 depend from and include every limitation of claim 1, which is described above.

DISCLOSURE OF THE CITED ART

Rettig *et al.* describes intramolecular rotation in *p*-cyano-*N,N*-dialkylanilines and its relation to the observed dual fluorescence in polar solvents. Among the compounds described in Rettig *et al.* is the compound 4-(2,5-dimethylpyrrolidin-1-yl)benzonitrile, which has the structure:



Rettig *et al.* does not disclose any compound that includes a 4-(pyrrolidin-1-yl)benzonitrile core structure substituted at position 3 of the aromatic ring with a non-hydrogen substituent.

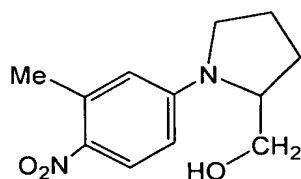
ANALYSIS

The cited compound of Rettig *et al.* is not within the scope of claims 5 and 17 or any pending claim. The compounds of instant formula II include a non-hydrogen substituent selected from among F, Cl, Br, I, OR^A, SR^A, NO₂, CN, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, COR^A, CO₂R^A, CONR^AR^B, SOR^A, SO₂R^A, and SO₂NR^AR^B, NHCOR^A, and NHCONR^AR^B at position 3 of the aromatic ring. The cited compound of Rettig *et al.* has a hydrogen substituent at the corresponding position.

None of the compounds of Rettig *et al.* has a non-hydrogen substituent selected from among F, Cl, Br, I, OR^A, SR^A, NO₂, CN, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, COR^A, CO₂R^A, CONR^AR^B, SOR^A, SO₂R^A, and SO₂NR^AR^B, NHCOR^A, and NHCONR^AR^B at position 3 of the aromatic ring. Thus, neither the cited compound of RN 80887-45-2 CAPLUS nor any compound described in Rettig *et al.* includes every element of claims 5 and 17. Therefore, Rettig *et al.* does not anticipate claims 5 or 17 or any pending claim.

3. Ohki *et al.*

Claims 6-11, 22-24 and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by RN 143525-57-9 CAPLUS (Ohki *et al.* (US 5,278,034), because Ohki *et al.* discloses the following compound:



Reconsideration of the grounds for the rejection respectfully is requested in view of the amendments herein and the following remarks.

RELEVANT LAW

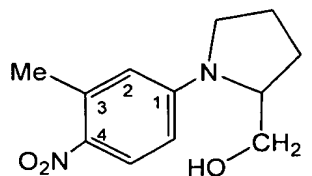
See related section above.

THE CLAIMS

Claims 6-11, 22-24 and 29 ultimately depend from and include every limitation of claim 1, which is described above.

DISCLOSURE OF THE CITED ART

Ohki *et al.* describes a process for forming a color photographic image that includes as a step developing an image-wise exposed silver halide color photographic material with a color developing composition containing an *N*-(4-aminophenyl)pyrrolidine derivative. Ohki *et al.* describes the synthesis of an *N*-(4-aminophenyl)pyrrolidine derivative that includes addition of pyrrolidin-2-ylmethanol to 4-fluoro-2-methyl-1-nitrobenzene to form (1-(3-methyl-4-nitrophenyl)pyrrolidin-2-yl)methanol, which has the structure:



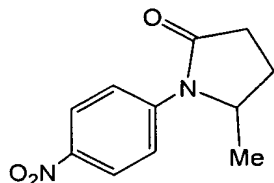
Ohki *et al.* does not disclose any compound that includes a 1-(4-nitrophenyl)pyrrolidine core structure substituted at position 3 of the aromatic ring with a non-hydrogen substituent selected from among F, Cl, Br, I, OR^A, SR^A, NO₂, CN, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, COR^A, CO₂R^A, CONR^AR^B, SOR^A, SO₂R^A, and SO₂NR^AR^B, NHCOR^A, and NHCONR^AR^B.

ANALYSIS

The cited compound of Ohki *et al.* is not within the scope of claims 6-11, 22-24 and 29 or any pending claim. The compounds of instant formula II include a non-hydrogen substituent selected from among F, Cl, Br, I, OR^A, SR^A, NO₂, CN, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, COR^A, CO₂R^A, CONR^AR^B, SOR^A, SO₂R^A, and SO₂NR^AR^B, NHCOR^A, and NHCONR^AR^B at position 3 of the aromatic ring. The cited compound of Ohki *et al.* has a methyl substituent at the corresponding position. None of the compounds of Ohki *et al.* has a non-hydrogen substituent selected from among F, Cl, Br, I, OR^A, SR^A, NO₂, CN, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, COR^A, CO₂R^A, CONR^AR^B, SOR^A, SO₂R^A, and SO₂NR^AR^B, NHCOR^A, and NHCONR^AR^B at position 3 of the aromatic ring. The majority of the compounds of Ohki *et al.* has a -NH₂ group at position 4, and thus are not within the scope of the instant claims. Thus, neither the cited compound of RN 143525-57-9 CAPLUS nor any compound described in Ohki *et al.* includes every element of claims 6-11, 22-24 and 29. Therefore, Ohki *et al.* does not anticipate any of claims 6-11, 22-24 and 29 or any pending claim.

4. Abdallah *et al.*

Claims 18-21, 25, 27, 28, 30 and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by RN 13691-23-1 CAPLUS (Abdallah *et al.* (Journal of the Chemical Society, Perkin Transactions 2: Physical Organic Chemistry (1972-1999) (8): 1243-1249 (1983))), because Abdallah *et al.* discloses the following compound:



Reconsideration of the grounds for the rejection respectfully is requested in view of the amendments herein and the following remarks.

RELEVANT LAW

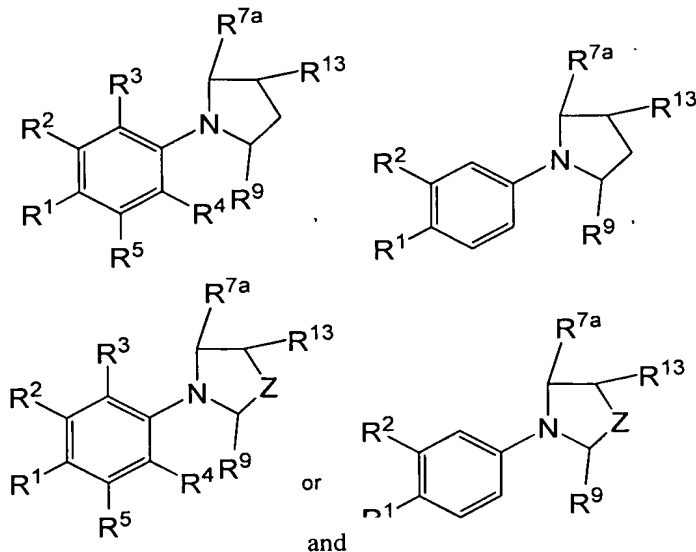
See related section above.

THE CLAIMS

Claims 18-21, 25, 27 and 28 ultimately depend from and include every limitation of claim 1, which is described above.

Claim 30 recites:

A compound that is selected from among:



where:

R¹ is selected from among SR^A, NO₂, CN, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, CO₂R^A, CONR^AR^B, SOR^A, and SO₂R^A;

R² is selected from F, Cl, Br, I, OR^A, SR^A, NO₂, CN, a substituted C₁-C₄ alkyl, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, COR^A, CO₂R^A, CONR^AR^B, SOR^A, SO₂R^A, and SO₂NR^AR^B, NHCOR^A, and NHCONR^AR^B;

R³, R⁴, and R⁵ each independently is selected from among hydrogen, F, Cl, OR^A, an optionally substituted C₁-C₄ alkyl, and an optionally substituted C₁-C₄ haloalkyl; provided that if R¹ is NO₂ and R³ is F, then Z is not O;

R^{7a} is selected from among hydrogen, an optionally substituted C₁-C₆ alkyl, an optionally substituted C₁-C₆ haloalkyl, an optionally substituted C₁-C₆ heteroalkyl, an optionally substituted C₂-C₆ alkynyl, and an optionally substituted C₂-C₆ alkenyl;

R⁹ is selected from an optionally substituted C₁-C₈ alkyl, an optionally substituted C₂-C₈ alkenyl, an optionally substituted C₁-C₈ haloalkyl, an optionally substituted C₂-C₈ haloalkenyl, C₁-C₈ heteroalkyl, an optionally substituted C₂-C₈ heteroalkenyl, an optionally substituted C₂-C₈ alkynyl, an optionally substituted C₂-C₈ haloalkynyl, an optionally substituted C₂-C₈ heteroalkynyl, an optionally substituted aryl, an optionally substituted heteroaryl, CH(R^D)OR^A, CH(R^D)NR^AR^B, COR^A, CO₂R^A, and (CH₂)_mR^C;

R¹³ is selected from among hydrogen, F, Cl, OR^A, NR^AR^B, SR^A, an optionally substituted C₁-C₆ alkyl, an optionally substituted C₁-C₆ haloalkyl, an optionally substituted C₁-C₆ heteroalkyl, an optionally substituted C₂-C₆ alkynyl, an optionally substituted C₂-C₆ alkenyl, and (CH₂)_mR^C;

R^A and R^B each independently is selected from among hydrogen, an optionally substituted C₁-C₄ alkyl, an optionally substituted C₁-C₄ haloalkyl, and an optionally substituted C₁-C₄ heteroalkyl;

R^C is selected from among an optionally substituted aryl and an optionally substituted heteroaryl that is optionally substituted with a substituent selected from among F, Cl, Br, I, CN, OR^A, NO₂, NR^AR^B, SR^A, SOR^A, SO₂R^A, an optionally substituted C₁-C₄ alkyl, an optionally substituted C₁-C₄ haloalkyl, and an optionally substituted C₁-C₄ heteroalkyl;

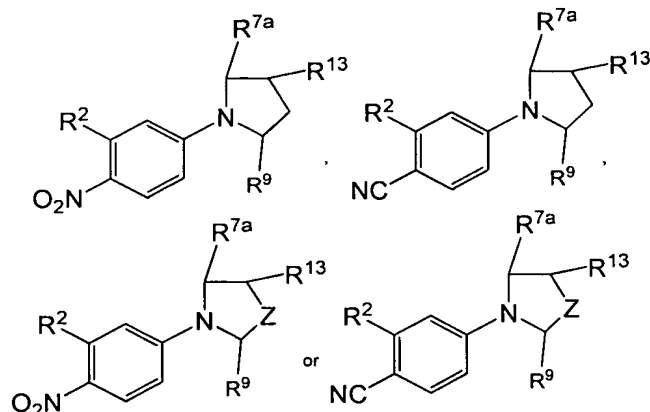
R^D is selected from among hydrogen, an optionally substituted C₁-C₄ alkyl, an optionally substituted C₁-C₄ haloalkyl, and an optionally substituted C₁-C₄ heteroalkyl;

Z is selected from among O, S, CR^AR^B, and NR^D; and

m is 1 or 2;

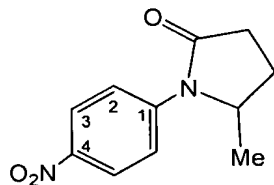
or a pharmaceutically acceptable salt, ester, or amide thereof.

Claim 35 depends from claim 30 and recites that the compound is:



DISCLOSURE OF THE CITED ART

Abdallah *et al.* describes the kinetics and equilibriums observed in ring closures through an amide linkage any hydrolytic ring closures in 1-aryl-2-pyrrolidones. Abdallah *et al.* describes the kinetics for 5-methyl-1-(4-nitrophenyl)-2-pyrrolidone, which has the structure:



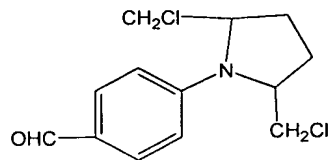
Abdallah *et al.* does not disclose any compound that includes a 4-(pyrrolidin-1-yl)-benzonitrile core structure substituted at position 3 of the aromatic ring with a non-hydrogen substituent.

ANALYSIS

The cited compound of Abdallah *et al.* is not within the scope of claims 18-21, 25, 27, 28, 30 and 35 or any pending claim. The compounds of instant formula II include a non-hydrogen substituent selected from among F, Cl, Br, I, OR^A, SR^A, NO₂, CN, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, COR^A, CO₂R^A, CONR^AR^B, SOR^A, SO₂R^A, and SO₂NR^AR^B, NHCOR^A, and NHCONR^AR^B at position 3 of the aromatic ring. The cited compound of Abdallah *et al.* has a hydrogen substituent at the corresponding position. None of the compounds of Abdallah *et al.* has a non-hydrogen substituent selected from among F, Cl, Br, I, OR^A, SR^A, NO₂, CN, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, COR^A, CO₂R^A, CONR^AR^B, SOR^A, SO₂R^A, and SO₂NR^AR^B, NHCOR^A, and NHCONR^AR^B at position 3 of the aromatic ring. Thus, neither the cited compound of RN 13691-23-1 CAPLUS nor any compound described in Abdallah *et al.* includes every element of claims 18-21, 25, 27, 28, 30 and 35. Therefore, Abdallah *et al.* does not anticipate any of claims 18-21, 25, 27, 28, 30 and 35.

5. Sokolov *et al.*

Claims 30-35 are rejected under 35 U.S.C. 102(b) as being anticipated by RN 10135-06-5 CAPLUS (Sokolov *et al.* (Zhurnal Obshchei Khimii 2(6): 1088-1092 (1966)), because Sokolov *et al.* discloses the following compound:



Reconsideration of the grounds for the rejection respectfully is requested in view of the amendments herein and the following remarks.

RELEVANT LAW

See related section above.

THE CLAIMS

Claims 30 and 35 are described above. Claims 31-34 depend from claim 30 and include every limitation thereof.

DISCLOSURE OF THE CITED ART

Sokolov *et al.* describes the synthesis of 2-amino-3-(4-(2,5-bis(chloromethyl)-pyrrolidin-1-yl)phenyl)propanoic acid using 2,5-bis(chloromethyl)-1-phenylpyrrolidine and (1-phenylpyrrolidine-2,5-diyl)dimethanol as starting materials. Among the intermediates produced in the synthesis described in Sokolov *et al.* is the compound 4-(2,5-bis(chloromethyl)-pyrrolidin-1-yl)-benzaldehyde, having the structure shown above.

Sokolov *et al.* does not disclose any compound that includes a 4-(pyrrolidin-1-yl)-benzonitrile core structure substituted at position 3 of the aromatic ring with a non-hydrogen substituent and at position 4 of the aromatic ring with a substituent selected from among SR^A , NO_2 , CN , an optionally substituted C_1 - C_4 haloalkyl, an optionally substituted C_1 - C_4 heteroalkyl, CO_2R^A , $CONR^AR^B$, SOR^A , and SO_2R^A as defined in claim 30.

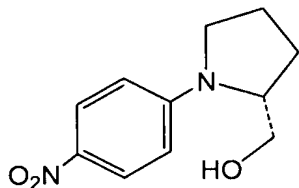
ANALYSIS

The cited compound of Sokolov *et al.* is not within the scope of claims 30-35 or any pending claim. The compounds of instant formula II include a non-hydrogen substituent selected from among F , Cl , Br , I , OR^A , SR^A , NO_2 , CN , an optionally substituted C_1 - C_4 haloalkyl, an optionally substituted C_1 - C_4 heteroalkyl, COR^A , CO_2R^A , $CONR^AR^B$, SOR^A , SO_2R^A , and $SO_2NR^AR^B$, $NHCOR^A$, and $NHCONR^AR^B$ at position 3 of the aromatic ring and include a non-hydrogen substituent selected from among SR^A , NO_2 , CN , an optionally substituted C_1 - C_4 haloalkyl, an optionally substituted C_1 - C_4 heteroalkyl, CO_2R^A , $CONR^AR^B$,

SOR^A, and SO₂R^A at position 4 of the aromatic ring. The cited compound of Sokolov *et al.* has a hydrogen substituent at position 3 and a -CHO substituent at position 4. None of the compounds of Sokolov *et al.* has a non-hydrogen substituent selected from among F, Cl, Br, I, OR^A, SR^A, NO₂, CN, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, COR^A, CO₂R^A, CONR^AR^B, SOR^A, SO₂R^A, and SO₂NR^AR^B, NHCOR^A, and NHCONR^AR^B at position 3 of the aromatic ring. None of the compounds of Sokolov *et al.* includes a non-hydrogen substituent selected from among SR^A, NO₂, CN, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, CO₂R^A, CONR^AR^B, SOR^A, and SO₂R^A at position 4 of the aromatic ring. Thus, neither the cited compound of RN 10135-06-5 CAPLUS nor any compound described in Sokolov *et al.* includes every element of claims 30-35. Therefore, Sokolov *et al.* does not anticipate any of claims 30-35.

6. Zyss *et al.*

Claim 62 is rejected under 35 U.S.C. 102(b) as being anticipated by RN 88422-19-9 (Zyss *et al.* (Journal of Chemical Physics 81(9): 4160-4167 (1984))), because Zyss *et al.* discloses the following compound:



Reconsideration of the grounds for the rejection respectfully is requested in view of the amendments herein and the following remarks.

RELEVANT LAW

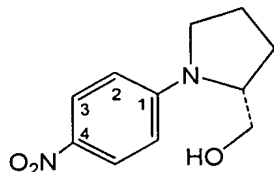
See related section above.

THE CLAIMS

Claim 62 depends from claim 1 and recites that the compound is selected from among:
(5*R*)-*N*-(4-nitrophenyl)-5-(dimethyl-tert-butylsilyloxymethyl)-2-pyrrolidone;
(2*R*)-*N*-(4-nitro-3-trifluoromethylphenyl)-2-(dimethyl-tert-butylsilyloxymethyl)-pyrrolidine;
(2*R*)-*N*-(4-nitro-3-trifluoromethylphenyl)-2-(hydroxymethyl)pyrrolidine;
(2*R*)-*N*-(3-Trifluoromethyl-4-nitrophenyl)-2-formylpyrrolidine;
(2*R*)-*N*-(3-Trifluoromethyl-4-nitrophenyl)-2-(1-(*S*)-hydroxy-2,2,2-trifluoroethyl)pyrrolidine;
(2*R*)-*N*-(3-Trifluoromethyl-4-nitrophenyl)-2-(1-(*R*)-hydroxy-2,2,2-trifluoroethyl)-pyrrolidine;
4-Benzyl-2-hydroxymethyl-1-(4-nitro-3-trifluoromethylphenyl)-pyrrolidine;
2-Fluoro-4-(2-hydroxymethyl-pyrrolidin-1-yl)-benzonitrile;
4-Hydroxy-1-(4-nitro-3-trifluoromethylphenyl)-pyrrolidine-2-carboxylic acid ethyl ester;
5-Hydroxymethyl-1-(4-nitro-3-trifluoromethylphenyl)-pyrrolidin-3-ol;
2-(Aminomethyl)-1-(4-Nitro-3-trifluoromethylphenyl)-pyrrolidine; and
4-Hydroxy-1-(4-nitro-3-trifluoromethylphenyl)-pyrrolidine-2-carboxylic acid;
and pharmaceutically acceptable salts, esters, and amides thereof.

DISCLOSURE OF THE CITED ART

Zyss *et al.* describes chiral hydrogen bonding nitroaniline derivatives for nonlinear optics. Among the compounds described in Zyss *et al.* is the compound *N*-(4-nitrophenyl)-(*L*)-prolinol, which has the structure:



Zyss *et al.* does not disclose any compound that includes a 1-(4-nitrophenyl)pyrrolidine core structure substituted at position 3 of the aromatic ring with a non-hydrogen substituent.

ANALYSIS

The cited compound of Zyss *et al.* is not within the scope of instant 62 or any pending claim. The compounds of instant formula II, including those recited in claim 62, include a non-hydrogen substituent selected from among F, Cl, Br, I, OR^A, SR^A, NO₂, CN, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, COR^A, CO₂R^A, CONR^AR^B, SOR^A, SO₂R^A, and SO₂NR^AR^B, NHCOR^A, and NHCONR^AR^B at position 3 of the aromatic ring. The cited compound of Zyss *et al.* has a hydrogen substituent at the corresponding position. None of the compounds of Zyss *et al.* has a non-hydrogen substituent selected from among F, Cl, Br, I, OR^A, SR^A, NO₂, CN, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, COR^A, CO₂R^A, CONR^AR^B, SOR^A, SO₂R^A, and SO₂NR^AR^B, NHCOR^A, and NHCONR^AR^B at position 3 of the aromatic ring. Thus, neither the cited compound of RN 88422-19-9 CAPLUS nor any compound described in Zyss *et al.* includes every element of claim 62. Therefore, Zyss *et al.* does not anticipate claim 62 or any pending claim.

II. THE REJECTION OF CLAIMS UNDER 35 U.S.C. §103(a)

Claims 30 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sokolov *et al.* (Zhurnal Obshchei Khimii 2(6): 1088-1092 (1966)) because Sokolov *et al.* teaches the compound 4-(2,5-bis(chloromethyl)pyrrolidin-1-yl)benzaldehyde, which the Examiner alleges is a positional isomer of the compounds of claim 33. The Examiner states that positional isomers, having the same radical on different positions of the molecule, are *prima facie* obvious, and require no secondary teaching because the experienced Ph.D. synthetic organic chemist would be motivated to prepare these positional isomers based on the

expectation that such close analogs would have similar properties and upon the routine nature of such positional isomer experimentation in the art.

Reconsideration of the grounds for the rejection respectfully is requested in view of the amendments herein and the following remarks.

RELEVANT LAW

For *prima facie* obviousness of claimed subject matter to be established under 35 U.S.C. §103, all the claim limitations must be taught or suggested by the prior art. In re Royka, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). This principle of U.S. law regarding obviousness was **not** altered by the Supreme Court holding in KSR International Co. v. Teleflex Inc., 127 S.Ct. 1727, 82 USPQ2d 1385 (2007). In KSR, the Supreme Court stated that “Section 103 forbids issuance of a patent when ‘the differences between the subject matter sought to be patented and the prior art are such the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.’” KSR Int'l Co. v. Teleflex Inc., 127 S.Ct. 1727, 1734, 82 USPQ2d 1385, 1391 (2007). The mere fact that prior art may be modified to produce the claimed product does not make the modification obvious unless the prior art suggests the desirability of the modification. In re Fritch, 23 U.S.P.Q.2d 1780 (Fed. Cir. 1992). Further, that which is within the capabilities of one skilled in the art is not synonymous with that which is obvious. Ex parte Gerlach, 212 USPQ 471 (Bd. APP. 1980).

Furthermore, the Supreme Court in KSR took the opportunity to reiterate a second long-standing principle of U.S. law: that a holding of obviousness requires the fact finder (here, the Examiner), to make explicit the analysis supporting a rejection under 35 U.S.C. 103, stating that “rejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness. Id. at 1740-41, 82 USPQ2d at 1396 (citing In re Kahn, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006)).

While the KSR Court rejected a rigid application of the teaching, suggestion, or motivation (“TSM”) test in an obviousness inquiry, the Court acknowledged the importance of identifying “a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does” in an obviousness determination. KSR, 127 S. Ct. at 1731. The court stated in dicta that, where there is a

“market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is

likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try **might** show that it was obvious under § 103.”

In a post-KSR decision, PharmaStem Therapeutics, Inc. v. ViaCell, Inc., 491 F.3d 1342 (Fed. Cir. 2007), the Federal Circuit stated that:

an invention would not be invalid for obviousness if the inventor would have been motivated to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. Likewise, an invention would not be deemed obvious if all that was suggested was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it.

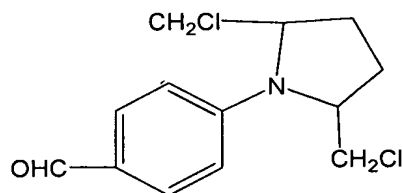
Furthermore, KSR has not overruled existing case law. See In re Papesch, (315 F.2d 381, 137 USPQ 43 (CCPA 1963)), In re Dillon, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1991), and In re Deuel (34 USPQ2d 1210, 1215 (Fed. Cir. 1995)). “In cases involving new compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish *prima facie* obviousness of a new claimed compound.” Takeda v. Alphapharm, 492 F.3d 1350, 1356-57 (Fed. Cir. 2007).

THE CLAIMS

Claim 30 is discussed in a related section above. Claim 33 depends from claim 30 and recites that R¹³ is an optionally substituted C₁-C₆ heterohaloalkyl.

The teachings of the cited art and differences from the claimed subject matter.

The teachings of Sokolov *et al.* are discussed in a related section above. Sokolov *et al.* teaches an intermediate in its synthetic schemes that has the structure:



Sokolov *et al.* does not teach or suggest any compound that includes a 4-(pyrrolidin-1-yl)-benzonitrile core structure substituted at position 3 of the aromatic ring with a non-hydrogen substituent and at position 4 of the aromatic ring with a substituent selected from among SR^A, NO₂, CN, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, CO₂R^A, CONR^AR^B, SOR^A, and SO₂R^A as defined in claim 30.

ANALYSIS

The compound 4-(2,5-bis(chloromethyl)pyrrolidin-1-yl)benzaldehyde mentioned in Sokolov *et al.* is not within the scope of claim 30 or 33 or any of the pending claims. Claims

30 and 33 recite that position 3 of the aromatic ring includes a non-hydrogen substituent selected from among F, Cl, Br, I, OR^A, SR^A, NO₂, CN, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, COR^A, CO₂R^A, CONR^AR^B, SOR^A, SO₂R^A, and SO₂NR^AR^B, NHCOR^A, and NHCONR^AR^B. The cited compound of Sokolov *et al.* has a hydrogen substituent at the corresponding position. None of the compounds of Sokolov *et al.* has a non-hydrogen substituent selected from among F, Cl, Br, I, OR^A, SR^A, NO₂, CN, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, COR^A, CO₂R^A, CONR^AR^B, SOR^A, SO₂R^A, and SO₂NR^AR^B, NHCOR^A, and NHCONR^AR^B at position 3 of the aromatic ring.

In addition, the compounds of claims 30 and 33 include a non-hydrogen substituent at position 4 of the aromatic ring that is selected from among SR^A, NO₂, CN, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, CO₂R^A, CONR^AR^B, SOR^A, and SO₂R^A, where R^A and R^B each independently is selected from among hydrogen, an optionally substituted C₁-C₄ alkyl, an optionally substituted C₁-C₄ haloalkyl, and an optionally substituted C₁-C₄ heteroalkyl. The cited compound of Sokolov *et al.* has a -CHO group at position 4. None of the compounds of Sokolov *et al.* includes a non-hydrogen substituent at position 4 of the aromatic ring that is selected from among SR^A, NO₂, CN, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, CO₂R^A, CONR^AR^B, SOR^A, and SO₂R^A as instantly claimed.

"In cases involving new compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish *prima facie* obviousness of a new claimed compound." Takeda v. Alphapharm, 492 F.3d 1350 (Fed. Cir. 2007). There is no teaching or suggestion in Sokolov *et al.* that would lead an ordinarily skilled chemist to take the 4-(2,5-bis(chloro-methyl)pyrrolidin-1-yl)-benzaldehyde intermediate of Sokolov *et al.* and replace the -CHO group at position 4 of the aromatic ring with a non-hydrogen substituent selected from among SR^A, NO₂, CN, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, CO₂R^A, CONR^AR^B, SOR^A, and SO₂R^A as instantly claimed, and to replace the hydrogen substituent at position 3 of the ring with a non-hydrogen substituent selected from among F, Cl, Br, I, OR^A, SR^A, NO₂, CN, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, COR^A, CO₂R^A, CONR^AR^B, SOR^A, SO₂R^A, and SO₂NR^AR^B, NHCOR^A, and NHCONR^AR^B, nor is there any teaching or suggestion that doing so would result in a compound having androgen receptor

modulating activity. Therefore, for at least these reasons, the Examiner has failed to set forth a *prima facie* case of obviousness of claims 30 and 33.

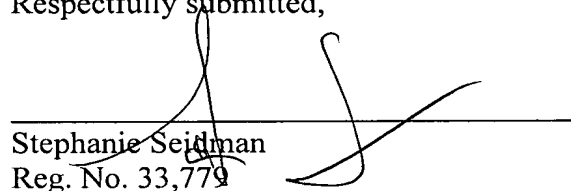
III. THE REJECTION OF CLAIMS UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claim 62 is rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and claim the subject matter. The Examiner alleges that the recitation “(compound ###)” renders the claim unclear “because the recitations appear to imply more than what is positively recited, since the name of the compound defines the compound.” Without acquiescing to or addressing the propriety of the rejection, in order to advance prosecution, claim 62 is amended to remove the compound numbers that follow the name of each compound. Thus, the amendment obviates the rejection.

* * *

In view of the amendment and remarks herein, entry of the amendment, reconsideration and allowance of the application respectfully are requested.

Respectfully submitted,



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